REMARKS/ARGUMENTS

Claim 1 is amended to incorporate the subject matter of claim 15 so as to be of the same scope as claim 15. Claims 15-19 are therefore canceled as being identical to claims 1-5 as now amended.

The method claims are amended to depend from claim 1 for the possibility of rejoinder.

The claims are rejected as obvious over Ogletree (US-6,509,348) in view of Bernat and, for some claims, further in view of Koike.

The present invention, as now claimed, is a pharmaceutical composition consisting essentially of CS-747 and aspirin in a ratio by weight of 1:500 to 500:1. The rejection is based on Ogletree for its teaching of a composition of three components: ADP receptor blocking antiplatelet drug (i.e. CS-747) in combination with thromboxane A_2 receptor antagonist and aspirin. Bernat is cited for teaching a pharmaceutical composition comprising an ADP receptor blocking antiplatelet drug (i.e. clopidogrel or ticlopidogrel) in combination with aspirin. Based on the teaching in Bernat, the Examiner considers it obvious to

use only two of the components in Ogletree (CS-747 and aspirin) and to exclude the thromboxane A_2 receptor antagonist. The Examiner considers that motivation to combine these references and make the modification exists because they are drawn to the same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem with which applicant is concerned.

Although the Examiner's reasoning may seem logical out of context of the art, within the context of the teaching of the art, it is submitted that the Examiner is using impermissible hindsight in making the combination. It is understood that there is always some hindsight involved in a rejection. However, when the art is specific concerning its teachings, a modification which is taught away from by the art, is not obvious. That is, it is submitted that a *prima facie* case of obviousness has not been made by the Examiner's rejection.

Concerning Ogletree, it is submitted that the teaching in Ogletree teaches away from leaving out the thromboxane A_2 receptor antagonist. Thus, for example, at column 4, starting at line 6, it states that the combination of ADP-receptor blocking antiplatelet drug and thromboxane A_2 receptor antagonist,

> "which works by a mechanism other than inhibition of ADP-induced platelet aggregation, is a surprising and unique concept in treating diseases involved with platelet aggregation, thrombus formation and ischemic events, in that the combination may provide additional antiplatelet aggregation, anti-ischemic, anti-thrombus effects over that which may be obtained using each of the components of the combination alone."

The disclosure further states that reduced levels of each of the two components may be employed to achieve desired results, albeit with reduced side effects. In other words, Ogletree is not just a combination of ADP-receptor blocking antiplatelet drug and thromboxane A_2 receptor antagonist (with aspirin an optional additive) but a combination of ADP-receptor blocking antiplatelet drug and thromboxane A_2 receptor antagonist to obtain a special effect. The aspirin is an optional additive. To remove one of the components is directly opposed to the basic invention of Ogletree, which requires that the two components with these specific mechanisms be used together. The special effect would be lost.

Ogletree further specifically states that aspirin is not substitutable for the other components because it works by a different mechanism. It is submitted that this teaches that aspirin is an optional ingredient that does not affect the

essential invention since it does not interact with the other components to provide the special effect (see column 4, lines 29-30 of Ogletree).

Considering Bernat, the Examiner's statement of the disclosure appears to refer to clopidogrel or ticlopidogrel (ticlopidine?) as equals. In fact, Bernat et al. considers aspirin and ticlopidin as prior art. The invention of Bernat is the use of clopidogrel with aspirin and is not a generic disclosure of the use of ADP-receptor blocking antiplatelet drugs. This can be seen from the disclosure at column 2, especially lines 48 et seq., where it points out that quite surprisingly and unexpectedly, "the clopidogrel-aspirin combination of the invention proved to be endowed with an synergistic activity of the two active ingredients." Substituting CS-747 for clopidogrel is not an obvious substitution in view of the teaching of this synergistic effect and the distinction of clopidogrel over another ADP receptor blocking antiplatelet drugs (ticlopidin). In summary, Ogletree teaches a special effect for two particular components and distinguishes aspirin as not one of those components (although it can be present). Bernat teaches clopidogrel and aspirin, and

distinguishes clopidogrel from another ADP-receptor blocking antiplatelet agent. To make the selection required for the rejection is to ignore the specific teachings in each of these references.

In view of the above, it is submitted that the Examiner has used impermissible hindsight to select completely out of context, that teaching which supports the rejection. Withdrawal of the rejection and allowance of the application on this basis alone is justified.

Applicants have provided test results showing that CS-747 with aspirin is surprisingly superior to clopidogrel and aspirin. In view of the disclosure in Bernat that clopidogrel provides a surprising and unexpected result as compared with another ADP receptor blocking antiplatelet drug, testing the inventive combination against the combination in the art which is described as providing a synergistic effect, is the closest prior art. The Examiner's position is that the testing should have been with respect to the presence and absence of the thromboxane A_2 receptor antagonist. However, this is tantamount to comparing apples with oranges. Ogletree states that there is a special effect from the combination of thromboxane A_2 and the ADP

receptor blocking antiplatelet drug. Ogletree also states that aspirin is not a substitute for the components required by Ogletree. Therefore, even if the three components of Ogletree were shown to provide better results than the present invention two components, the present invention would still be unexpected since Ogletree teaches a different mechanism of operation and Bernat teaches an expectation that clopidogrel provides the best results in combination with aspirin. Under the facts here, this is clearly the closest art. Comparing different mechanisms of combinations (e.g. Ogletree vs. the present invention) is not a reasonable comparison and should not be required.

It is therefore submitted that the test data of record shows an unexpected effect for the present invention (CS-747 plus aspirin) over the closest appropriate prior art (clopidogrel plus aspirin) and supports withdrawal of the rejection and allowance of the application.

Koike is relied upon to show salts and does not otherwise modify the teaching so as to effect the arguments presented hereinabove.

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In view of the above, withdrawal of the rejection and allowance of the application are respectfully requested.

Respectfully submitted,

Frishauf, Holtz, Goodman
& Chick, P.C.
220 Fifth Ave., 16th Floor
New York, NY 10001-7708
Tel. No. (212) 319-4900
Fax No.: (212) 319-5101
MJC/ld

MARSHALL J. CHICK
Reg. No. 26,853